Tuberculosis in Immigrants to Canada

A Global Problem Which Requires a Global Solution

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Tuberculosis has, for most of the 20th century, been on the decline in the industrialized world. At the same time, the disease has dramatically increased in the majority of the world's population who live in the developing world.^{1,2} Tuberculosis was declared a 'global emergency' by the World Health Organisation in 1993 at a time when many Western countries were talking about the impending elimination of the disease. The low level of concern about the disease that this engendered in the Western world contributed to the lack of progress in the development of new approaches and tools to control tuberculosis.³ Also responsible was the unfounded confidence that the development in the 1970s of efficacious 'short course' treatment regimens would, given time, resolve the problem of tuberculosis. The results of the few effectiveness studies using these regimens under program conditions failed to raise the alert that short-course regimens were not, in reality, having their desired effect.⁴ For example, a 6-month regimen tested by the British Medical Research Council in East Africa, using subjects selected for compliance and treated largely in hospital, had a relapse rate of 9%⁵ while under program conditions, the same regimen had a relapse rate of 25%.⁴ The widespread introduction of these treatment regimens without an adequate infrastructure probably increased the infective pool by decreasing the mortality but not increasing the cure of tuberculosis.⁶ Furthermore, the inappropriate use of antituberculosis drugs has progressively increased the prevalence of resistant strains of *Mycobacterium tuberculosis*.^{6,7}

Against the background of declining interest in and dismantling of programs for tuberculosis in the industrialized countries, there has been a steady increase in emigration from high prevalence to low prevalence tuberculosis countries.¹ In areas in the industrialized world favoured by immigrants and where the matter has been studied, tuberculosis in foreign-born accounts for most of the disease. In Canada, 58% of all tuberculosis occurs in foreign-born⁸ while in the southern part of the province of Alberta, foreign-born accounted for 17% of the population and 71% of the tuberculosis in the period 1990 to 1995.⁹ In Canada it has been proposed that the population be supplemented with approximately 250,000 immigrants per year; this could lead to an annual increase rather than the hoped for decrease in the incidence of tuberculosis.

Tuberculosis in foreign-born is often caused by *Mycobacterium tuberculosis* which is resistant to one or more of the conventional antituberculosis drugs.¹⁰ Resistant *Mycobacterium tuberculosis* is three times more common in foreign-born than it is in Canadian-born with tuberculosis.¹¹ Disease caused by resistant *Mycobacterium tuberculosis* is more difficult to treat and has greater morbidity and mortality than disease caused by a susceptible organism.¹²

The Canadian preimmigration screening program emphasizes tuberculosis by including a history of past tuberculosis and, for all potential immigrants over 11 years of age, a chest x-ray. Those found to have active pulmonary tuberculosis are denied immigration until their disease has been proved to be inactive by adequate treatment and follow-up. Those

judged to have inactive pulmonary tuberculosis are required to attend for tuberculosis assessment after their arrival in Canada. In a paper in this issue of the Journal, Uppaluri and colleagues from Ontario report that this surveillance process identified only 14% of the immigrants who subsequently were diagnosed with tuberculosis.¹³ Their finding is similar to that reported in a survey of tuberculosis in immigrants to southern Alberta in which the immigration process identified 10% of those who subsequently developed tuberculosis.⁹ In both of these reports, the impact of treatment of latent tuberculosis infection (chemoprophylaxis) was disappointing, pointing to poor compliance either on the part of the physicians or the patients. Poor compliance is the major problem with chemoprophylaxis and may be particularly poor in foreign-born populations.¹⁴ The current guidelines suggest that all immigrants 35 years of age or less, with tuberculin reactions of 10 mm or greater, who come from high prevalence countries should be offered chemoprophylaxis with isoniazid.¹⁵ Half of the immigrants, all from countries with a high incidence of tuberculosis, who developed tuberculosis in southern Alberta⁹ and 60% of those in Canada⁸ were under 35 years of age at the time of their arrival in Canada and might thus have been eligible for chemoprophylaxis. Although the risk of isoniazid-induced liver toxicity increases significantly above the age of 35 years,¹⁶ those below that age, especially women and particularly those who are in the first year post-partum, may be at increased risk with four times more deaths than men of the same age.¹⁷ Severe side effects and death have been reported in recent reports, one from Canada associated with isoniazid¹⁸ and another from the USA in association with a 'short-course' regimen with rifampin and pyrazinamide.¹⁹ The data from follow-up of population groups in Canada demonstrate that isoniazid chemoprophylaxis might cause more cases of serious side-effects or even deaths than the number of cases of tuberculosis prevented when used in those with a positive tuberculin test and no other risk factors for developing tuberculosis.²⁰ This opinion has previously been presented by others,²¹ and is supported by the observation that the incidence of tuberculosis in the Canadian immigrant population is only 20 per

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100,000 per year.⁸ A recent Canadian study has estimated that chemoprophylaxis is cost effective only for immigrants from countries with a high prevalence of tuberculosis who have abnormalities on their pre-immigration chest x-rays and not when provided on the basis of only a positive tuberculin skin test.²²

Given the small impact of pre-immigration screening and the problems associated with preventive therapy in immigrants to Canada, the definitive way to decrease tuberculosis in the foreign-born is to decrease the prevalence of disease in their countries of origin.^{3,23} The industrialized world has the resources and the expertise to provide the relatively inexpensive and extremely cost-effective tuberculosis programs needed in these countries. Indeed Zumla and Grange suggest that it is morally wrong to do otherwise.²⁴ This view is supported by a recent paper in which the inequalities of wealth and of health services across the regions of the world are emphasized and we are urged to think 'about local and international activities that have the potential to improve well-being and health at the global level'.²⁵

Canada is a signatory to the recent 'G8 Communiqué Okinawa 2000' in which the eight major industrialized democracies pledged to 'reduce TB deaths and prevalence of the disease by 50% by 2010'. This Communiqué resurrects the spirit of the World Health Organisation's Alma-Ata declaration of 'Health for All by the Year 2000',²⁶ and we should pursue and attempt to exceed this goal in the context of tuberculosis.

In conclusion, if we are to control and eventually eradicate tuberculosis in Canada, we need to address the disease in our foreign-born population. The current screening programs detect only 10 to 14% of those immigrants who subsequently develop tuberculosis. Current chemoprophylaxis policies are ineffective and expensive. Our goal to eradicate tuberculosis in Canada can be best achieved by the development of new programs and the release of new resources. Ideally, and ultimately, these new programs must address tuberculosis in the world and not be local, expensive and largely cosmetic operations.

REFERENCES/RÉFÉRENCES

1. Rieder HL. *Epidemiologic Basis of Tuberculosis Control*. Paris: IUATLD, 1999.
2. Dye C, Scheele S, Dolin P, Pathania V, Ravignione MC. Global burden of tuberculosis. Estimated incidence, prevalence, and mortality by country. *JAMA* 1999;282:677-86.
3. Grange JM. Paradox of the global emergency of tuberculosis. *Lancet* 1999;353:996.
4. Cowie RL, Langton ME, Becklake MR. Pulmonary tuberculosis in South African gold miners. *Am Rev Respir Dis* 1989;139:1086-89.
5. East African/British Medical Research Council. Controlled clinical trial of four short-course regimens of chemotherapy for two durations in the treatment of pulmonary tuberculosis. *Am Rev Respir Dis* 1978;118:39-48.
6. Medical Research Council. Streptomycin treatment of pulmonary tuberculosis. *BMJ* 1948;ii:769-83.
7. Mitchison DA. Drug resistance in mycobacteria. *Br Med Bull* 1984;40:84-90.
8. Long R, Njoo H, Hershfield E. Tuberculosis: 3. Epidemiology of the disease in Canada. *CMAJ* 1999;160:1185-90.
9. Cowie RL, Sharpe JW. Tuberculosis among immigrants: Interval from arrival in Canada to diagnosis. A 5-year study in southern Alberta. *CMAJ* 1998;158:599-602.
10. Manns BJ, Fanning EA, Cowie RL. Antituberculosis drug resistance in immigrants to Alberta, Canada, with tuberculosis, 1982-1994. *Int J Tuberc Lung Dis* 1997;1:225-30.
11. Long R, Fanning A, Cowie R, Hoepfner V, Fitzgerald M. Antituberculous drug resistance in western Canada (1993 to 1994). *Can Respir J* 1997;4:71-76.
12. Mitchison DA, Nunn AJ. Influence of initial drug resistance on the response to short-course chemotherapy of pulmonary tuberculosis. *Am Rev Respir Dis* 1986;133:423-30.
13. Uppaluri A, Naus M, Heywood N, Brunton J, Kerbel D, Wobeser W. Effectiveness of the immigration medical surveillance program for tuberculosis in Ontario. *Can J Public Health* 2002;93(2):88-91.
14. Nolan CM, Aitken ML, Elarth AM, Anderson KM, Miller WT. Active tuberculosis after isoniazid chemoprophylaxis of Southeast Asian refugees. *Am Rev Respir Dis* 1986;133:431-35.
15. Long R (Ed.). *Canadian Tuberculosis Standards* 5th ed. Canadian Lung Association, 2000.
16. Kopanoff DE, Snider DE, Caras GJ. Isoniazid-related hepatitis. *Am Rev Respir Dis* 1978;117:991-1001.
17. Snider DE, Caras GJ. Isoniazid-associated hepatitis deaths: A review of the available information. *Am Rev Respir Dis* 1992;145:494-97.
18. Turner MO, Elwood RK. Severe hepatic complications of antituberculous therapy. *Can J Infect Dis* 1999;10:167-69.
19. Centers for Disease Control and Prevention. Update: Fatal and severe liver injuries associated with rifampin and pyrazinamide for latent tuberculosis infection, and revisions in American Thoracic Society/CDC recommendations - United States, 2001. *Am J Respir Crit Care Med* 2001;164:1319-29.
20. Enarson DA. Screening for tuberculosis infection and disease. *Monaldi Arch Chest Dis* 1998;53:144-47.
21. Comstock GW, Edwards PQ. The competing risks of tuberculosis and hepatitis for adult tuberculin reactors. *Am Rev Respir Dis* 1975;111:573-77.
22. Schwartzman K, Menzies D. Tuberculosis screening of immigrants to low-prevalence countries. *Am J Respir Crit Care Med* 2000;161:780-89.
23. Zuber PL, McKenna MT, Binkin NJ, Onorato IM, Castro KG. Long-term risk of tuberculosis among foreign-born persons in the United States. *JAMA* 1997;278:304-7.
24. Zumla A, Grange JM. Establishing a united front against the injustice of tuberculosis. *Int J Tuberc Lung Dis* 1998;2:179-81.
25. Benatar SR. Respiratory health in a globalizing world. *Am J Respir Crit Care Med* 2001;163:1064-67.
26. Declaration of Alma-Ata. International Conference on Primary Health Care, 6-12 September 1978, Alma-Ata, USSR. World Health Organisation, Geneva.

ÉDITORIAL

La tuberculose chez les immigrants au Canada

Un problème global qui exige une solution globale

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Pour l'essentiel du 20^e siècle, on peut dire que la tuberculose a beaucoup diminué dans le monde industrialisé. Parallèlement, on a constaté une augmentation alarmante de la maladie au sein des populations vivant dans le tiers monde.^{1,2} En 1993, l'Organisation mondiale de la Santé a déclaré que la tuberculose constituait une « urgence mondiale », à une époque où bon nombre de pays occidentaux envisageaient la disparition

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Unlike many other provinces in Canada, Ontario does not have centralized TB clinics. As a result, high-risk immigrants may be evaluated in the primary care setting. Physicians who may have relatively little understanding of TB may be the only decision-makers in the evaluation and management of such persons. A surveillance system in which few high-risk patients are offered a risk-reducing intervention is highly unlikely to be cost-effective,¹¹ and may lead to an erroneous belief that the risk of TB transmission is being adequately managed. Timely and adequate medical evaluation and follow-up of immigrants who are at high risk for the reactivation of TB can have a relatively high yield.^{2,5,10,12,17} Failing to provide effective surveillance may place the Canadian population at risk.

REFERENCES

- Cowie RL, Sharpe JW. Tuberculosis among immigrants: Interval from arrival in Canada to diagnosis. A 5-year study in southern Alberta. *CMAJ* 1998;158(5):599-602.
- Orr PH, Manfreda J, Hershfield ES. Tuberculosis surveillance in immigrants to Manitoba. *Can Med Assoc J* 1990;144:553-58.
- Ormerod LP. Tuberculosis screening and prevention in new immigrants 1983-88. *Respir Med* 1990;84(4):269-71.
- National Guidelines for the Investigation and Follow-up of Individuals Who Were Placed Under Surveillance for Tuberculosis After Arrival in Canada. *Canadian Tuberculosis Standards* 5th edition. Canadian Lung Association, 2000; Appendix A:229-35.
- Wang JS, Allen EA, Enarson DA, Grzybowski S. Tuberculosis in recent Asian immigrants to British Columbia, Canada: 1982-1985. *Tubercle* 1991;72(4):277-83.
- Zuber PL, McKenna MT, Binkin NJ, Onorato IM, Castro KG. Long-term risk of tuberculosis among foreign-born persons in the United States. *JAMA* 1997;278(4):304-7.
- Wobeser W, Yuan L, Naus M, Corey P, Edelson J, Heywood N, et al. Expanding the epidemiologic profile - Risk factors for active tuberculosis among persons immigrating to Ontario. *CMAJ* 2000;163(7):823-30.
- American Thoracic Society. Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection. *MMWR* 2000;49(RR-6).
- Hoepfner V, Marciniuk D, Hershfield E. Treatment of Tuberculosis Disease and Infection. *Canadian Tuberculosis Standards* 5th edition. Canadian Lung Association, 2000;83-111.
- Verver S, Bwire R, Borgdorff MW. Screening for pulmonary tuberculosis among immigrants: Estimated effect on severity of disease and duration of infectiousness. *Int J Tuberculosis Lung Disease* 2001;5(5):419-25.
- Dasgupta K, Schwartzman K, Marchand R, Tennenbaum TN, Brassard P, Menzies D. Comparison of cost-effectiveness of tuberculosis screening of close contacts and foreign-born populations. *Am J Respir Crit Care Med* 2000;162(6):2079-86.
- Carlos EK, Cantwell MF, Bhatia G, Gedin G, Lewis J, Mohle-Boetani JC. Public health interventions to encourage TB class A/B1/B2 immigrants to present for TB screening. *Am J Respir Crit Care Med* 1998;158(4):1037-41.
- Menzies D, Adhikari N, Tannenbaum T. Patient characteristics associated with failure of tuberculosis prevention. *Tuber Lung Dis* 1996;77(4):308-14.
- Centers for Disease Control. Recommendations for prevention and control of tuberculosis among foreign born persons. *MMWR* 1998;47(RR-16).
- Heath TC, Roberts C, Winks M, Capon AG. The epidemiology of tuberculosis in New South Wales 1975-1995: The effects of immigration in a low prevalence population. *Int J Tuberc Lung Dis* 1998;2(8):647-54.
- MacIntyre CR, Plant AJ, Streton JA, Yung A. Missed opportunities for prevention of tuberculosis in Victoria, Australia. *Int J Tuberc Lung Dis* 1997;1(2):135-41.
- Wells CD, Zuber PL, Nolan CM, Binkin NJ, Goldberg SV. Tuberculosis prevention among foreign-born persons in Seattle-King County, Washington. *Am J Respir Crit Care Med* 1997;156(2 Pt 1):573-77.
- Nolan C. Community-wide implementation of targeted testing for and treatment of latent tuberculosis infection. *Clin Infect Dis* 1999;29(4):880-87.

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RÉSUMÉ

Contexte : Le ministère de la Citoyenneté et de l'Immigration (CIC) prévoit un dépistage de la tuberculose chez les immigrants et autorise les personnes atteintes de tuberculose pulmonaire latente à entrer au Canada à condition qu'elles se soumettent à une surveillance médicale. Nous avons étudié ce programme en Ontario.

Méthode : Nous avons recoupé les données nationales et provinciales d'une base de données de gestion.

Résultats : En 1994-1995, on a diagnostiqué 1 341 cas de tuberculose active dans la population née à l'étranger, et 1 095 de ces cas étaient répertoriés par CIC. Notre analyse a porté sur 142 des 149 personnes (14 %) placées sous surveillance médicale par CIC. Une proportion significative de ces personnes (39/142 : 27 %) avaient été diagnostiquées avant ou durant le dépistage exigé par l'immigration. Elles étaient entrées au Canada en qualité de visiteurs ou de réfugiés. Seules 21 des 103 personnes restantes (20 %) ayant fait l'objet d'un dépistage de l'immigration avant leur diagnostic de tuberculose respectaient l'obligation de se soumettre à une surveillance médicale. La plupart (82/103 : 82 %) présentaient des symptômes, mais 1 seule des 16 personnes admissibles (6 %) était traitée pour une tuberculose latente, ce qui suggère que la tuberculose a pu se propager en Ontario.

Interprétation : Le système de surveillance de la tuberculose en vigueur en Ontario pour les immigrants très vulnérables ne parvient pas à détecter et à traiter les infections latentes, ni donc à prévenir les cas futurs.

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Zumla et Grange vont même jusqu'à dire que ne pas le faire est immoral.²⁴ On retrouve ce même point de vue dans un article récent qui fait ressortir les inégalités dans la richesse et les services de santé selon les régions du monde et dans lequel nous sommes invités à réfléchir « aux activités locales et internationales susceptibles d'améliorer le bien-être et la santé au niveau mondial ». ²⁵

Le Canada est signataire du récent « Communiqué Okinawa 2000 du G8 » dans lequel les huit principales démocraties

du monde industrialisé s'engagent à « réduire la morbidité due à la tuberculose et la prévalence de la maladie de 50 % d'ici 2010 ». Ce Communiqué relance l'esprit de la Déclaration d'Alma Ata de l'Organisation mondiale de la Santé, « La Santé pour tous en l'an 2000 », ²⁶ et nous devrions nous efforcer de dépasser cet objectif s'agissant de la tuberculose.

En conclusion, si l'on veut contrôler et finalement éradiquer la tuberculose au Canada, il faut s'attaquer à la maladie au sein de la population immigrée. Les programmes actuels de dépistage ne permettent de détecter que de 10 à 14 % des

immigrants qui plus tard développeront la maladie. Les politiques de chimioprophylaxie actuelles sont chères et inefficaces. Notre objectif d'éradication de la tuberculose au Canada sera plus facilement atteint en mettant au point de nouveaux programmes et en débloquent de nouveaux crédits. Dans le meilleur des cas, et en définitive, ces nouveaux programmes doivent s'attaquer à la tuberculose dans le monde et ne pas être de simples opérations locales, coûteuses et largement superficielles.